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Observation of conformational exchange in cyclosporin in media of varying polarity by NMR spectroscopy

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Abstract

© Springer-Verlag Wien 2014. The molecule of peptide cyclosporin A experiences chemical exchange in polar solvents. In apolar media, such as chloroform or benzene, this transformation is suppressed, but still leads to formation of a small fraction of a minor conformer. To elucidate the nature of this phenomenon, the peptide was dissolved in mixed solvents chloroform–DMSO and water–DMSO. Analysis of 1H nuclear magnetic resonance and two-dimensional exchange spectroscopy spectra showed that the conformational exchange proceeds at a low rate of ~10-1 s-1 at the room temperature and involves passing over a high free energy barrier. Thus the situation resembles the exchange process in chloroform, associated with cis–trans isomerization of peptide bonds, but in the presence of DMSO transformation occurs at several sites independently, and the energy difference between arising conformers is small, 102–103 kJ/mol.

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